196), Lol p 5B (Q40237) (SEQ ID NO: 197), Lol p 5A (Q9XF24) (SEQ ID NO: 198), Lol p 5 C (Q9SC99) (SEQ ID NO: 199), Phl p 5.0206 (OB1343) (SEQ ID NO: 200), Hol I 5 (O23972) (SEQ ID NO: 201), Phl p 5.0207 (OB1344) (SEQ ID NO: 202), Hol I 5B (AAG42255) (SEQ ID NO: 203), Poa p 5 (AAG42254) (SEQ ID NO: 204), Phl p 5.0203 (OB1342) (SEQ ID NO: 205), Phl p 5 (P93466) (SEQ ID NO: 206), Phl p 5B (Q40963) (SEQ ID NO: 207), Phl p 5.0204 (Q9SBE0) (SEQ ID NO: 208), Phl p 5.02 (O23971) (SEQ ID NO: 209), Pha a 5.3 (P56166) (SEQ ID NO: 210), Pha a 5.1 (HAAQ) (SEQ ID NO: 211), Hor v 9 (O04828) (SEQ ID NO: 212) and Hor v 5 (30kDa) (Q39995) (SEQ ID NO: 213).--

IN THE CLAIMS

Claims 36, 40-42, 45 and 46 have been cancelled, without prejudice or disclaimer.

Claims 68-85 have been added.

Claims 2-8, 10-18, 30, 33, 35, 37-39, 43, 44, 47-55, 58-61, 64 and 65 have been amended as follows:

--2. (Amended) A recombinant allergen according to claim 1, wherein the primary mutations are spaced between about 20 [Å, preferably 25 Å and most preferably] to 30 Å.

3. (Amended) A recombinant allergen according to claim 1 [or 2] comprising a number of secondary mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the binding capability of the said naturally occurring allergen, wherein each secondary mutation is a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, wherein the secondary mutations are placed outside the said circular region.

4. (Amended) A recombinant allergen according to [any of claims 1-3] claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 20 %[, preferably above 30 %, more preferably above 40 % and most preferably above 50 %].

5. (Amended) A recombinant allergen according to [any of claims 1-4] claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 70 %[, preferably 80 % and most preferably 90 %] identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

6. (Amended) A recombinant allergen according to [any of claims 1-5] claim 1, which essentially has the same α-carbon backbone tertiary structure as said naturally occurring allergen.

7. (Amended) A recombinant allergen according to [any of claims 1-6] claim 1, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic genus[, preferably the subfamily, more preferably the family, more preferably the superfamily, more preferably the legion, more preferably the suborder and most preferably the order] from which said naturally occurring allergen originates.

8. (Amended) A recombinant allergen according [to any of claims 1-7] claim 1, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 5%[, preferably at least 10%].

10. (Amended) A recombinant allergen according to [any of claim 1-9] claim 1, characterised in that said circular surface region comprises atoms of 15-25 amino acid residues.

11. (Amended) A recombinant allergen according to [any one of claims 1-10] claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to solvent accessibility, and that one or more amino acids among the more solvent accessible ones are substituted.

12. (Amended) A recombinant allergen according to [any one of claims 1-11] claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to degree of [conversation] conservation in all known homologous proteins within the species from

which said naturally occurring allergen originates, and that one or more amino acids among the more conserved ones are substituted.

13. (Amended) A recombinant allergen according to [any of claims 1-12] claim 1, wherein the mutant allergen is a non-naturally occurring allergen.

14. (Amended) A recombinant allergen according to [any of claims 1-13] claim 1 comprising from 5 to 20[, preferably from 6 to 15, more preferably from 7 to 12, and most preferably from 8 to 10] primary mutations.

15. (Amended) A recombinant allergen according to [any one of claims 1-14] claim 3 characterised in that the mutant allergen comprises from 1 to 4 secondary mutations per primary mutation.

16. (Amended) A recombinant allergen according to [any one of claims 1-15] claim 1, characterised in that one or more of the substitutions is carried out by site-directed mutagenesis.

17. (Amended) A recombinant allergen according to [any one of claims 1-16] claim 1, characterised in that one or more of the substitutions is carried out by DNA shuffling.

18. (Amended) A recombinant allergen according to [any one of claims 1-17] claim 1, characterised in that it is a mutant of an inhalation allergen.

30. (Amended) A recombinant allergen according to [any one of claims 1-17] claim 1 characterised in that it is a mutant of a venom allergen.

33. (Amended) A recombinant allergen according to [any one of claims 30-32] claim 30 characterised in that it is a mutant of Ves v 5.

35. (Amended) A pharmaceutical composition comprising the recombinant allergen according to[any of claims 1-34 for use as] claim 1 and at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

37. (Amended) A composition comprising two or more recombinant mutant allergen variants according to [any of claims 1-34] claim 1, wherein each variant is defined by having at least one primary mutation, which is absent in at least one of the other variants, wherein for each variant no secondary mutation is present within a radius of 15 Å from each absent primary mutation.

38. (Amended) A composition according to claim 37 comprising 2-12[, preferably 3-10, more preferably 4-8 and most preferably 5-7] variants.

39. (Amended) A composition according to claim 37 [or 38 for use as a pharmaceutical] further comprising at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

43. (Amended) A method of generating an immune response in a subject comprising administering to the subject a recombinant allergen according to [any one of] claim[s] 1-[34,] or a composition according to any one of claims 35, 37 or 39 [38 or a pharmaceutical composition according to claims 41 or 42].

44. (Amended) A method of vaccinating [Vaccination or treatment of] a subject comprising administering to the subject a recombinant allergen according to [any one of] claim[s] 1[-34,] or a composition according to any one of claims 35, 37 or 39 [38 or a pharmaceutical composition according to claims 41 or 42].

47. (Amended) A method for the treatment, prevention or alleviation of allergic reactions in a subject comprising administering to a subject a recombinant allergen according to [any one of] claim[s] 1[-34,] or a composition according to any one of claims 35, 37 or 39 [38 or a pharmaceutical composition according to any one of claims 41-42 or 46].

48. (Amended) A method of preparing a recombinant allergen according to [any one of claims 1-34] claim 1, [characterised in] comprising

a) identifying a number of amino acid residues in a naturally occurring allergen, which have [has] a solvent accessibility of at least 20%;

b) selecting at least four of the identified amino acid residues in such a manner that each selected amino acid is spaced from each other selected amino acid by at least 15 Å, and that the selected amino acids are placed in such a manner that at least one circular surface region with an area of 800 $Å^2$ comprises no selected amino acid; and

c) effecting for each of the selected amino acids a primary mutation, which reduces the specific IgE binding capability of the mutated allergen as compared to the binding capability of the said naturally occurring allergen, wherein each primary mutation is a substitution of a selected amino acid residue with another amino acid, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates.

49. (Amended) A method according to claim 48, characterised in ranking [the] said identified amino acid residues with respect to solvent accessibility and substituting one or more amino acids among the more solvent accessible ones.

50. (Amended) A method according to claim 48 [or 49], characterised in selecting identified amino acid residues, which are conserved with more than 70 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

51. (Amended) A method according to claim 50, characterised in ranking [the] said identified amino acid residues with respect to degree of [conversation] conservation in all known homologous proteins within the species from which said naturally occurring allergen originates and substituting one or more amino acids among the more conserved ones.

52. (Amended) A method according to [any of claims 48-51] claim 48 comprising selecting the identified amino acids so as to form a mutant allergen, which has essentially the same α-carbon backbone tertiary structure as said naturally occurring allergen.

53. (Amended) A method according to [any of claims 48-52] claim 48 characterised in that the substitution of amino acid residues is carried out by site-directed mutagenesis.

54. (Amended) A method of preparing a recombinant allergen according to [any one of claims 1-34] claim 1 comprising [, characterised in that the allergen is produced from a DNA sequence obtained by] DNA shuffling (molecular breeding) of the DNA encoding the corresponding naturally occurring allergen to produce said recombinant allergen.

55. (Amended) A DNA sequence encoding a recombinant allergen according to [any of claims 1-34] claim 1, a derivative thereof, a partial sequence thereof, a degenerated sequence thereof or a sequence, which hybridises thereto under stringent conditions, wherein said derivative, partial sequence, degenerated sequence or hybridising sequence encodes a peptide having at least one B cell epitope.

58. (Amended) A DNA sequence according to [any of claims 55-57] claim 56, wherein the sequence is a derivative of the sequence shown in Fig. 3, wherein the DNA sequence [is mutated so as to] encodes an allergen having at least four mutations selected from the group consisting of V2, D72, E87, K-129, E-60, N-47, K-65, P-108, N-159, D-93, K-123, K-32, D-125, R-145, D-109, E-127, Q-36, E-131, L-152, E-6, E-96, D-156, P-63, H-76, E-8, K-134, E-45, T-10, V-12, K-20, S-155, H-126, P-50, N-78, K-119, V-2, L-24, E-42, N-4, A-153, I-44, E-138, G-61, A-130, R-70, N-28, P-35, S-149, K-103, Y-150, H-154, N-43, A-106, K-115, P-14, Y-5, K-137, E-141, E-87 and E-73.

59. (Amended) A DNA sequence according to [any of claims 55-57] claim 56, wherein the sequence is a derivative of the sequence shown in Fig. 13, wherein the DNA sequence [is mutated so as to] encodes an allergen having at least four mutations selected from the group consisting of K-16, K-185, K-11, K-44, K-210, R-63, K-13, F-6, K-149, K-128, E-184, K-112, F-157, E-3, K-29, N-203, N-34, K-78, K-151, L-15, L-158, Y-102, W-186, K-134, D-87, K-52, T-67, T-125, K-150, Y-40, Q-48, L-65, K-81, Q-101, Q-208, K-144, N-8, N-70, H-104, Q-45, K-137, K-159, E-205, N-82, A-111, D-131, K-24, V-36, N-7, M-138, T-209, V-84, K-172, V-19, D-56, P-73, G-33, T-106, N-170, L-28, T-43, Q-114, C-10, K-60, N-31, K-47, E-5, D-145,

V-38, A-127, D-156, E-204, P-71, G-26, Y-129, D-141, F-201, R-68, N-200, D-49, S-153, K-35, S-39, Y-25, V-37, G-18, W-85 and I-182.

60. (Amended) A DNA sequence according to [any of claims 55-57] claim 56, wherein the sequence is a derivative of the sequence shown in Fig. 16, wherein the DNA sequence [is mutated so as to] encodes an allergen having at least four mutations selected from the group consisting of R-128, D-129, H-11, H-30, S-1, K-77, Y-75, R-31, K-82, K-6, K-96, K-48, K-55, K-89, Q-85, W-92, I-97, H-22, V-65, S-24, H-74, K-126, L-61, P-26, N-93, D-64, I-28, K-14, K-100, E-62, I-127, E-102, E-25, P-66, L-17, G-60, P-95, E-53, V-81, K-51, N-103, Q-2, N-46, E-42, T-91, D-87, N-10, M-111, C-8, H-124, I-68, P-79, K-109 and R-128, D-129, H-11, H-30, S-1, K-77, Y-75, R-31, K-82, K-6, K-96, K-48, K-55, K-89, Q-85, W-92, I-97, H-22, V-65, S-24, H-74, K-126, L-61, P-26, N-93, D-64, I-28, K-14, K-100, E-62, I-127, E-102, E-25, P-66, L-17, G-60, P-95, E-53, V-81, K-51, N-103, Q-2, N-46, E-42, T-91, D-87, N-10, M-111, C-8, H-124, I-68, P-79, K-109 and K-15.

61. (Amended) An expression vector comprising the DNA according to any one of claims 55-60 operably linked to a promoter.

64. (Amended) A recombinant allergen according to [any of claims 1-34 or encoded by the DNA sequence according to any of claims 55-60] claim 1 comprising at least one T cell epitope capable of stimulating a T cell clone or T cell line specific for the naturally occurring allergen.

65. (Amended) A diagnostic assay for assessing relevance, safety or outcome of therapy of a subject using a recombinant mutant allergen according to claim1, comprising [any of claims 1-34 or a composition according to claim 37 or 38, wherein an IgE containing sample of the subject is mixed with said mutant or said composition and] assessing[ed for] the level of reactivity between [the] IgE in [said] a sample from said subject and said mutant allergen. --